Translation

PCT/JP2004/000629

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference E1-A0211P	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/JP2004/000629	International filing date (*day/month/year*) 23 January 2004 (23.01.2004)	Priority date (*day/month/year*) 24 January 2003 (24.01.2003)
International Patent Classification (IPC) or national classification and IPC C12N 15/09, C07K 16/28, C12N 5/08, C12P 21/08, C12Q 1/68, 1/02, G01N 33/50, 33/53, A61P 25/00		
Applicant EISAI CO., LTD.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:

      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☒ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) DISC 1, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

   ☒ Box No. I Basis of the report
   ☐ Box No. II Priority
   ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   ☐ Box No. IV Lack of unity of invention
   ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   ☐ Box No. VI Certain documents cited
   ☐ Box No. VII Certain defects in the international application
   ☒ Box No. VIII Certain observations on the international application

Date of submission of the demand 29 July 2004 (29.07.2004)	Date of completion of this report 27 December 2004 (27.12.2004)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2004/000629

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ The international application as originally filed/furnished

☐ the description:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

pages _____, as originally filed/furnished

pages* _____, as amended (together with any statement) under Article 19

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the drawings:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2004/000629

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1, 3-5, 7, 8	YES
	Claims	2, 6	NO
Inventive step (IS)	Claims	1, 3-5	YES
	Claims	2, 6-8	NO
Industrial applicability (IA)	Claims	1-8	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Document 1: WO 99/64608 A1 (Schering AG) December 16, 1999
& EP 1084259 A1 & JP 2002-517253 A
Document 2: WO 01/057194 A2 (Corvas International Inc.) August 9, 2001
& EP 1252300 A2 & US 2003/0119168 A1 & JP 2003-521920 A
Document 3: Eur. J. Biochem., Vol. 267, No. 23, pp 6931-6937 (2000)
Document 4: WO 00/06700 A1 (Layton Bioscience Inc.) February 10, 2000
& EP 1109887 A1
Document 5: US 6277820 B1 (Genentech Inc.) August 21, 2001

Claim 2

Based on the descriptions in documents 1-3 cited in the international search report, the invention of claim 2 lacks novelty and an inventive step.

Document 1 describes antibodies to human and murine Corin (equivalent to Lrp4/Corin in the present application); document 2 describes antibodies to the human type II membrane serine protease MTSP (equivalent to Lrp4/Corin in the present application); and document 3 describes antibodies to human corin (equivalent to Lrp4/Corin in the present application).

Claim 6

Based on the descriptions in documents 4 and 5 cited in the international search report, the invention of claim 6 lacks novelty and an inventive step.

Document 4 describes a process for differentiating dopamine-producing neurons from precursor cells using differentiation inducing agents such as retinoic acid, etc.; and document 5 describes a process for differentiating dopamine-producing neurons from precursor cells using sonic hedgehog.

Claims 7, 8

Based on the description in Document 4 cited in the international search report, the inventions of claims 7 and 8 lack an inventive step.

Document 4 describes a process for differentiating dopamine-producing neurons from precursor cells using differentiation inducing agents such as retinoic acid, etc., and the differentiation of neurons is monitored using the detection of tyrosine hydroxylase and bc1-2 production. Therefore, the detection of genes and chemical substances associated with differentiation and induction are obvious to persons skilled in the art.

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The invention of claim 1 describes a base sequence containing 15 bases associated with a base sequence hybridized under stringent conditions with the base sequence of SEQ ID NO: 1 or 2, but the fact that a polynucleotide isolated from the base sequence of SEQ ID NO: 1 or 2 can be used to detect dopamine-producing neurons is not fully supported by the Description.

The invention of claim to describes an antibody to a polypeptide having a polypeptide of 8 amino acid residues associated with Lrp4/Corin. The fact that this kind of short fragment can detect dopamine-producing neurons is not fully supported by the Description.

Supplemental Box Relating to Sequence Listing

Continuation of Box No. 1, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis that of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☐ in written format

   ☒ in computer readable form

   c. time of filing/furnishing

   ☐ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purpose of search and/or examination

   ☐ received by this Authority as an amendment* on _____

2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

** If item 4 in Box No. I applies, the listing and /or table(s) related thereto, which form part of the basis of the report, may be marked "superseded".*

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of Box V:

Claims 1 and 3-5

The inventions of claims 1 and 3-5 are novel and involve an inventive step with respect to the documents cited in the international search report.

These documents do not state that the Lrp4/Corin identified as SEQ ID NO: 1-4 is specifically expressed in dopamine-producing neuron proliferation precursor cells. Moreover, persons skilled in the art cannot easily conceive of that matter.